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ORIGINAL ARTICLES.

PAROXYSMAL PULMONARY ŒDEMA AND ITS TREATMENT.

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The condition designated paroxysmal pulmonary œdema cannot well be mistaken for any other. It comes on very suddenly with little or no premonitory indication and rapidly assumes such alarming characters that the patient and those about him feel that a fatal termination can be a matter of but few minutes. The patient at the very beginning experiences a sense of suffocation or oppression of breathing which speedily becomes extreme. He struggles for breath, and soon becomes additionally oppressed by paroxysms of suppressed cough in which a little frothy and often blood-tinged serous fluid is brought up. Later, larger quantities of the same sort of frothy serum may be expectorated or may literally well up from the lungs. The breathing is merely moist on auscultation or noisy, according to the degree of œdema; in severe attacks it becomes suppressed. When the frothy expectoration has stood for a time in a vessel the bubbles of air disappear, leaving a clear and usually blood-tinged serous fluid.

At the moment of the attack the patient grows suddenly deathly pale and wears the anxious expression of terror of one who fears instant death. The hands, feet, and whole body grow cold and become bathed in a dripping sweat. Later, as the respirations grow more and more difficult, cyanosis becomes associated with the pallor. Extreme cyanosis, however, is uncommon. The pulse, usually extremely weak and rapid in the beginning, may continue so until some relief is afforded. In some of the seizures in cases reported in this series the pulse during the early part of the paroxysm was almost imperceptible, and improved very gradually as the attack subsided. Occasionally, however, the pulse may be rapid and excited during an attack and may give no evidence of reduced cardiac power. It will be shown later that even in such cases the actual working power of the left ventricle may be diminished, and that the mechanical conditions capable of developing pulmonary œdema may be present despite the seeming strength of the pulse.

At the beginning of the attack the patient is usually nervous and frightened, and this condition may increase with the oppressed breathing and suffocating cough. Later, a certain amount of stupor or partial unconsciousness may develop, but this is unusual. After a time the patient grows easier; warmth returns to the hands, which have been cold and cyanosed; the breathing improves; the moist rales in the chest grow less abundant; color returns to the face; and the pulse grows stronger and less frequent. The majority of paroxysms terminate in this way; in but a small proportion of cases does a fatal termination occur, notwithstanding the extreme violence of the symptoms usually observed. Some patients have, however, died in the first attack; others have survived for a period of months or years, despite repeated seizures. In Lissaman's[1] case there were seventy-two attacks during a period of over two years; and the patient was living at the time of the report. In one of my cases paroxysms have occurred at intervals of weeks or months during the last ten years; and the patient is now in rather better physical condition than after the first attack in 1900.

The distinguishing features, clinically speaking, of the condition that has been referred to are its sudden onset, usually with slight provocation; the evidence of intense pulmonary œdema; the expectoration of quantities of frothy and blood-stained serum; and the repetition of such attacks without intercurrent complicating conditions. These features distinguish this condition from certain other forms of acute pulmonary œdema, which, during their height, may not be especially different in clinical manifestations.

The seizures, as a rule, come on in the evening or after the patient has gone to bed. He may awake from a profound sleep with an oppressed cough, followed by the symptoms described. In some cases, vague apprehensions or unaccountable nervous feelings may precede the attack; but these usually occur only after a repetition of the seizures has made the patient familiar with their character and fearful of their recurrence. Various kinds of excitement, physical or mental, may provoke the attacks; but in a large proportion of cases there is no such cause.

Repeated attacks of the same character may occur at intervals of days or weeks during a long period of time. In one of my cases the seizures began over ten years ago and have continued up to the present time at varying intervals. Between attacks the patient may be perfectly well, or more frequently give evidence of some inadequacy of cardiac compensation. In the cases which have terminated fatally the final result has usually been due to increasing cardiac decompensation rather than to the sudden effect of an attack of pulmonary œdema.

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[1] Lancet, February 8, 1902.

It is necessary to point out here some of the other varieties of acute pulmonary œdema met with clinically, so that the limitations of what is intended to be included under the title paroxysmal pulmonary œdema may be more evident.

1. ACUTE ŒDEMA ASSOCIATED WITH OTHER LESIONS OF THE LUNGS. It is a well-known fact that cases of pneumonia or pulmonary tuberculosis may terminate suddenly by the development of an acute œdema affecting a part or all of the lung not involved in the original trouble. The explanation offered for such cases by older writers, and to a large extent still accepted, is that there is a collateral hyperemia or fluxion, resulting from the extent of the original trouble. Another explanation is, however, possible, particularly in cases of acute pneumonia. This is that, as a result of dissemination of the infective cause, an acute inflammatory œdema of the entire lung or of both lungs follows after the original infection. In this condition, there may be a close resemblance in the symptoms to what has been described before; but the history of the case and the circumstances under which the acute œdema arises distinguish this from paroxysmal œdema.

2. ACUTE INFECTIOUS ŒDEMA; ACUTE INFLAMMATORY ŒDEMA; OR ACUTE ŒDEMATOUS INFLAMMATION. This condition, which was originally described by Traube as serous pneumonia, or diffuse congestive pneumonia, may occur in association with certain infectious diseases, such as scarlet fever, smallpox, typhus fever, rheumatism, or influenza, or as a primary infection of the lungs. Its resemblance to vagus pneumonia is too close to be overlooked; and its occurrence in cases of acute cerebral disease, head injuries, or sunstroke is likewise suggestive. Strümpell[2] alludes to such cases, and mentions the absence of other lesions than the œdematous lung. Hilton Fagge[3] and Fowler[4] describe the same condition. Sahli[5] insists that this is purely an infectious condition; and Kockel,[6] in his pathological and bacteriological study of 6 cases following head injury, found a constant association of bacterial invasion and the acute inflammatory lesions. He further states that Thoma believes that most diffuse or extensive œdemas are inflammatory and infectious, and mentions that Ziegler describes

[2] Text-book on Medicine, second American edition, p. 183.

[3] Text-book on Medicine, third edition, i, 1002.

[4] Diseases of the Lungs, p. 281.

[5] Archiv f. exper. Pharm. u. Path., 1885, 19.

[6] Deut. Naturf. und Aerzte, 1896, lxviii, 30.

such cases as "septic-toxic" œdema. Welch[7] states that he agrees with Sahli regarding the frequency of infectious inflammatory pulmonary œdemas, basing his opinion upon the systematic bacterial examinations made at all autopsies at the Johns Hopkins Hospital. Not only in irregular and localized œdemas, but also in not a few extensive and even general ones, plate cultures from the lungs showed numerous colonies of bacteria, most frequently streptococci and lanceolate micrococci, so numerous that they must have been in active growth in the lungs. Sudden œdema associated with Bright's disease, described by Dieulefoy[8] and by other French writers, may, in some cases, belong in this same group, but is possibly susceptible of another explanation, similar to that which will be suggested in the case of paroxysmal œdema.

The clinical manifestations of acute infectious œdema, as I have seen them in some cases of influenza and other infections, do not differ greatly from those of paroxysmal pulmonary œdema, except that there is much less suddenness and vehemence of the symptoms. Certain authors (as Romberg) have mentioned as distinguishing features the fact that there is fever in these cases, and usually a pulse suggestive of increased rather than lessened cardiac action; and undoubtedly these are important points, and may lead to a proper diagnosis. It must, however, be recalled that fever is not invariably present, and that in some instances of paroxysmal pulmonary œdema the pulse-rate does not give evidence of decided cardiac weakness. A more important criterion for distinguishing the two conditions is the tendency to recurrence in the one and the absence of such a tendency in the other. Furthermore, paroxysmal pulmonary œdema, as will be pointed out later, occurs in association with certain other conditions, cardiovascular or renal, and rarely independently of such causes; while infectious œdema may appear in persons previously in perfect health. Later, in the discussion of the pathogenesis of the pulmonary condition in paroxysmal cases, I shall have occasion to point out that infection has been thought of as the important etiological factor. A series of paroxysms would, therefore, necessarily imply a series of successive infections. Such an occurrence is manifestly most unlikely, and all the facts connected with the recurrent paroxysms in cases such as those observed by myself over long periods of time speak strongly against this possibility.

3. ACUTE ŒDEMA ACCOMPANYING RAPID DILATATION OF THE HEART. In cases of acute dilatation of the heart caused by acute myocarditis or degeneration of the heart, considerable œdema of the lungs may develop quite rapidly; and the clinical features at the height of such an attack may be indistinguishable from those

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[7] Quoted by Meltzer, "Œdema," American Medicine, viii, Nos. 1 to 5.

[8] Path. Int., thirteenth edition, T. I., i, 282.

which occur in seizures of paroxysmal œdema such as have been described. The manner of onset and the coincident conditions, however, distinguish such cases from the paroxysmal type; for there is usually a clear history of preceding acute cardiac weakness, and, perhaps, even prior to that, of some infection which has occasioned it. Then, too, physical signs of increasing cardiac weakness and of increasing dilatation of the heart precede the onset of the pulmonary œdema. Thus, it is usually possible to distinguish the two conditions, notwithstanding the fact that at the height of the symptoms they are practically indistinguishable, as cardiac dilatation quite commonly occurs as an incident of the attack in the paroxysmal variety.

While we may thus recognize four types of sudden, or acute, œdema of the lungs, it must be apparent that the first is clearly distinguished from the others mainly by its recurrent character; and for this reason, I have ventured to use the term *paroxysmal pulmonary œdema*. Among other names that have been suggested is acute suffocative pulmonary œdema, but this is less descriptive, because practically all forms of acute œdema are almost equally suffocative in character.

A report of some typical cases will serve to indicate the clinical features.

Case I.—Mr. E. B., aged seventy years, at the time of his death, in May, 1909, had been under my observation for six or eight years. He had formerly been addicted to the overuse of alcohol, and was an inveterate smoker. He came of a distinctly gouty family, and he himself suffered from a moderate obesity and later from a mild glycosuria which came and went. During the time he was under my observation I recognized the development of increasing arteriosclerosis, and examinations of the urine showed traces or small quantities of albumin and tube casts significant of an increasing interstitial nephritis. The blood pressure was constantly high, and increased with succeeding years. During the last four years of his life the sugar had disappeared from the urine. None was present from January, 1905, up to the time of his death.

The first attack of pulmonary œdema occurred during the winter of 1908, after a somewhat heavy dinner. The patient had gone to the theatre, and while there complained of the heat of the room and of oppression of breathing. He was quickly hurried out before the attack developed, but he could not get to his home, and when I reached him, fifteen minutes later, in an adjoining house, where he had been taken, I found him in the midst of an attack of the most intense severity. The pulse was scarcely palpable, the face was livid, and the skin everywhere icy cold and bedewed with dripping perspiration. The breathing was noisy and the lungs were evidently œdematous throughout. A physician who had seen him before my arrival had given him a pearl of nitrite of amyl, which was inhaled from a handkerchief with apparently some slight relief. I gave him a hypodermic injection of morphine with atropine, and in a short time he was sufficiently restored to be taken home; but subsequent hypodermic injections of strychnine, nitroglycerin, and atropine were given, as the patient was greatly exhausted. After an hour he fell asleep, and the next day was practically well though much exhausted. After this attack the patient had a succession of similar seizures, probably fifteen in all, none, however, of the intensity of the first, and in each of these the prompt administration of hypodermic injections of morphine, sometimes with and sometimes without atropine, relieved him speedily. The general course of his case, however, was a downhill one, and finally increasing œdema and other evidences of cardiac failure terminated the condition. Toward the end it seemed to me as if he might perish in one of the attacks on account of his generally weakened condition and the progressive deterioration of cardiac strength, but there never was any difficulty in controlling the seizures themselves. The final outcome of the case and the progress was practically the same as that of a case of general arteriosclerosis with cardiac disease unattended with such paroxysms of pulmonary œdema.

CASE II.—Mrs. H. E. R., now aged fifty years, first came under my observation in December, 1900. She had had a severe attack of cardiac disturbance of some sort a short time before that date, and when I first saw her she was still suffering from some of the consequences of a disturbance or a loss of compensation. The principal symptoms were dyspnœa, cough, and other indications of pulmonary congestion. On physical examination I found slight enlargement of the heart and the evidences of mitral stenosis. After the administration of moderate doses of cardiac tonics, compensation became restored and the patient was quite well until February, 1902, when a sudden attack of intense congestion and œdema of the lungs with cardiac weakness occurred in the middle of the night. Another attack occurred in March, 1902, after which she remained free of seizures, although at times not entirely well, until the spring of 1906, when she was greatly reduced by hemorrhoidal bleeding, and in May she had another severe attack of acute œdema. The fifth attack occurred during the summer of 1906, the seventh about six weeks later, the eighth and ninth in October and December of 1908, the tenth in October, 1909, and the eleventh on January 28, 1910. All of these attacks have been of similar character and all occurred during the night. In several the direct cause was sexual excitement. In others the patient has been wakened from sleep with a frightened feeling, which was quickly followed by intense oppression of breathing, a rattling sound in the chest, great weakness and rapidity of the pulse, and the expectoration of more or less copious amounts of frothy and usually blood-tinged serum. Since the first attack, and up to the latest one, she has had the prompt attendance of a physician, who administered hypodermic injections of morphine with small amounts of atropine, and the result has invariably been a speedy recovery after a single hypodermic dose. In the last attack strychnine and nitroglycerin were used, and though the patient recovered from the attack, the duration was somewhat longer than on previous occasions, and the attack was one of no great severity, having been attended with but little œdema and no frothy expectoration. The first attack of all was described as the most severe of the series, but I cannot give any details regarding it. After the attacks the patient quickly regains her normal condition, but during the ten years she has been under my care there has been the constant evidence of a cardiac defect with slight dyspnœa on exertion and a lowered general vitality. There has been no evidence of progressive loss of power in the heart, and the patient's general condition now is apparently quite as satisfactory as it was in the beginning. The physical signs of mitral stenosis, as is so common in cases of that lesion, are more distinct in the intervals between than during or immediately following attacks. Urinary examinations have shown a slight trace of albumin on a few occasions, but not more than might be attributed to the leukocytes present as a result of some vesical trouble. The latest examination made on the day following her attack of January 28 showed: specific gravity 1018, reaction acid, no albumin, no sugar, no cylindroids or casts, a number of leukocytes, and some uric acid crystals. There has never been any indication in the urinary examinations or symptoms of nephritis.

Case III.—I. K., aged fifty years, first came under my care in 1901. He had used alcohol periodically to great excess, but not at all during the last year and never subsequently up to the time of his death in 1909. He had, however, continued smoking immoderately, and never limited this at all reasonably until near the end of his life. In 1902 he suffered from an attack of abdominal pain which Dr. J. Chalmers Da Costa and I regarded as due to appendicitis, but we decided it safer to avoid operation on account of certain cardiac symptoms. For some time previous to this date the patient had complained of substernal and precordial oppression, especially on slight exertion, as in walking up moderate hills on his golf course. The pulse was constantly rapid, and more so when he was specially oppressed. The heart sounds were weak but sharp, and the aortic second sound slightly accentuated. There was no cardiac enlargement and no murmur. In 1904 he had considerable anginoid pain, and in the summer another attack of what was regarded as appendicitis. Early in 1905 he had another abdominal attack, with pain most marked in the epigastrium.

Soon after this he complained of a severe headache or neuralgia, which was followed by right homonymous hemianopia affecting the right upper quadrant. Dr. de Schweinitz saw him and reported the condition "right lateral homonymous tetranopia." The vision improved after some time and possibly as a consequence of the use of potassium iodide. Another abdominal attack occurred later in 1905. In the meantime, his precordial distress never was wholly relieved, though it was less severe or he had grown accustomed to it. During the summer of 1907 he had one or two attacks of severe cardiac distress while at some altitude in the Adirondack mountains; and in the spring of 1908 he had the first attack of threatening character. The description of the seizure, given by a friend who was with him, corresponded in every detail with that which would apply to subsequent attacks which I observed. A pellet of morphine and one of nitroglycerin were given, and after some hours relief occurred. I saw the patient the next day and found him in his usual condition, though somewhat used up by his experience of the night before. The cardiac signs were the same as those described. On the following night another attack occurred, and in this he developed a complete right hemiplegia with aphasia. Up to this time I had not seen the patient in an attack, but during the following eighteen months I saw him in several, and in others Dr. Klaer was called.

There was usually little premonition of the attack, but a certain amount of nervousness and mild oppression preceded the paroxysm for a short time. The attack itself set in very suddenly with extreme oppression of breathing, violent palpitation with great weakness of the heart beat and pulse, ashy pallor combined with some cyanosis, and cold sweat. Very soon he would begin to cough in short interrupted paroxysms, bringing up frothy serous fluid of pink color, and in bad seizures the same kind of frothy fluid flowed from his mouth between the coughing attacks. At the height of the attack the lungs were filled throughout with moist rales and the entrance of air was reduced to a minimum. Scarcely any inspiration or expiration could be distinguished.

During the eighteen months following the hemiplegia there were twelve such attacks or distinct beginnings of attacks and a number of milder suggestions. He was under the constant care of a nurse, who had been instructed to give a hypodermic injection of morphine, $\frac{1}{4}$ grain, and atropine, $\frac{1}{250}$ grain, at the first sign of a seizure, to be followed by one of strychnine sulphate, $\frac{1}{20}$ grain, and nitroglycerin, $\frac{1}{100}$ grain, within ten or fifteen minutes, and a repetition of morphine, $\frac{1}{8}$ grain, with atropine, $\frac{1}{250}$ grain, after a half hour if necessary. This plan never failed to abort the attacks within a few minutes and without any actual need for the second or third injection. In two or three of the attacks, when the nurse or members of the family thought the first symptoms merely nervousness, the attacks got greater headway and relief did not occur as speedily, but even then the patient was relieved in a half hour. The effect of the injections was to cause a rapid improvement in the oppression of breathing, followed by a fuller pulse, returning warmth of the extremities, and diminution in the frothy expectoration. The last four attacks occurred during the summer in Atlantic City, and Dr. Porteous reports that these were of the same character as previous ones, and up to the last one were controlled by a moderately large hypodermic dose of morphine and atropine, which on one or two occasions had to be repeated. The last and fatal attack differed only in being more severe than any previous ones Dr. Porteous had seen. It began while the patient was in a theatre, and possibly the delay in applying treatment may have been responsible for the fatal result. There was no autopsy.

Case IV.—W. H. S. was admitted to my service at the University Hospital in February, 1905, on account of cough, expectoration, and occasional hemoptysis. The patient was a shipper, aged twenty-two years, who had suffered from articular rheumatism four years ago, had been a moderate user of alcohol and tobacco, but without any other significant history. At this time signs of aortic regurgitation and mitral stenosis were discovered and a suspicious lesion was found at the apex of the left lung. We were never certain that this was a tuberculous lesion, as examination for bacilli was always negative and the cardiac condition could have easily occasioned a localized area of congestion. The patient left the hospital in April and was treated at a sanatorium for tuberculosis, where he remained until September, 1905, having gained considerably in weight, and being then discharged as cured. He attempted to resume his work, but soon noticed a return of blood-tinged sputum, and reëntered the hospital in the fall of 1907, with practically the same conditions we had previously found. The patient, however, had increased greatly in weight from the forced feeding, and we were under the impression that this increased weight had exaggerated rather than helped his cardiac difficulties. After a month's stay in the hospital he felt quite well, and was about to go home, when some little excitement incident to his departure from the hospital caused a sudden attack of acute œdema. He had walked from the ward to the elevator, and there was seized with intense dyspnœa and weakness, and was carried back to his bed. A severe attack of acute œdema followed, the respirations increasing to 50, the pulse to 160 per minute. Considerable frothy material welled out of his mouth and he was extremely cyanosed. Repeated injections of camphorated oil, digitalin, and atropine were given. Of the last, doses of $\frac{1}{80}$ grain were given every thirty minutes during four hours, but the attack did not subside for eight hours, after which there was a slight improvement. During this attack it was noted that the cardiac dulness increased to the left as well as to the right, and as the patient improved the following day this increased dulness seemed to diminish. A second attack occurred two weeks later, and was described as a very severe one. The symptoms were the same as those in the previous seizure. A hypodermic injection of morphine and atropine followed by digitalin and camphorated oil quickly terminated this attack, and the patient's condition was practically normal within a few hours. Five days later a third attack occurred, and promptly yielded to a single injection of morphine and atropine. Three more seizures followed at intervals of a few weeks, after which the patient had no further attacks of this sort. He subsequently developed a fresh cardiac infection with pericarditis, and eventually succumbed to this. Repeated examinations of the urine showed either an absence of albumin or mere traces, and sometimes a few hyaline casts, but more often none at all.

CASE V.—J. G., aged sixty-one years, had first come under my observation early in 1908, after an attack of cardiac palpitation and dyspnœa which had come on during the night. He was sent to the University Hospital, where he has been a patient off and on up to the present time. Examination showed evidences of general arteriosclerosis and chronic interstitial nephritis. The peripheral vessels are sclerosed and tortuous. The blood pressure has varied from 200 to 240 mm. systolic, and 130 to 145 mm. diastolic. There is more or less constant polyuria, and the examinations have shown traces of albumin with hyaline and granular casts. Since his first admission to the hospital there have been a number of attacks similar to the one he described as having occurred before admission. The first of these which occurred in the hospital is described as follows: "The patient was suddenly seized with an attack starting with eructations, followed in a short time by coughing and expectoration of frothy material. Dyspnœa became very marked, making it impossible for him to breathe unless sitting up in bed. A hypodermic injection of morphine caused a relief, but a return of the attack required a second injection." All the subsequent attacks have been similar to this. Their onset has been sudden and without marked premonition. The lungs quickly become moist and breathing seriously oppressed. A hypodermic injection of morphine with atropine quickly terminates the seizures.

On account of the renal condition, the patient has had constant hot packs at intervals of two or three days, and his general condition has remained practically stationary. Lately, however, a slight increase in the frequency of the attacks has been noted, and their sharp demarcation from his average condition has been less distinct, as the breathing remains somewhat oppressed and the lungs slightly congested between the seizures. Some tests as to the relative value of injections of morphine and of morphine and atropine in the recent paroxysm seem to show a moderate advantage in the latter over the former.

The progress of this case has been from a condition of practical comfort for long stretches punctuated by sudden intense seizures, from which the patient quickly returned to his usual condition, to one of more frequent but less severe attacks with a more lasting state of pulmonary congestion and œdema between the paroxysms.

ETIOLOGY. The explanation of paroxysms of sudden pulmonary œdema may be sought (1) in a study of the conditions in which such paroxysms have been encountered, and (2) in the experimental and physiological data bearing upon the question.

1. *Associated Pathological Conditions.* Several authors have summarized the literature of acute pulmonary œdema, and have made tables of the various conditions with which it was associated. Samuel West[9] mentions as a rough classification of the causes of acute œdema: (1) Acute inflammation; (2) acute collateral fluxion; (3) sudden mechanical obstruction to the vessels; (4) acute fevers; (5) certain poisons; (6) hyperpyrexia; (7) acute nephritis; and (8) paracentesis thoracis; and in the detailed discussion of these groups speaks of various diseases which fall under one or the other of the headings. Riesman[10] mentions, among the associated conditions in reported cases, arteriosclerosis, Bright's disease, heart disease, asthma, acute infectious diseases, pregnancy, paracentesis of the thorax and of the abdomen, angioneurotic œdema, obscure conditions of questionable relationship (hysteria, etc.).

It is evident that the acute œdema which occurs in some of these conditions is not strictly comparable to the paroxysmal type which is under discussion. Thus, the sudden œdema occurring after paracentesis or in some violent infection, such as scarlet fever, very probably results from different causes than those which are operative in the cases in which one paroxysm after another has occurred more or less spontaneously. To say the least, there must be an added factor of etiology that determines such recurrences of œdema, and more probably the etiology is entirely different. In the case of infectious acute œdema, for example, it is very probable that the direct action of the microörganisms upon the pulmonary vessels and the adjacent tissues is the immediate cause, and it is inconceivable that repeated attacks of paroxysmal œdema are due to repeated acute infections. The same thought applies to the probable mechanical disturbances operative in the œdema following paracentesis. It is necessary, therefore, to distinguish the conditions with which acute œdema has been associated as a recurring paroxysmal event from those in which there have been only single attacks. Little help in the direction of solving the question of the etiology of the œdema in the paroxysmal type of cases can be expected from mere tabulations of all the pathological conditions in which any sort of sudden pulmonary œdema occurred; but in studying the detailed descriptions of the cases which have been reported and upon which the tables are based, the paroxysmal type stands out very prominently. Taking this group alone, it is found that practically all of the cases were instances of cardiac or renal disease, or arteriosclerosis. Young persons without any of these conditions may suffer infectious pulmonary œdema, collateral œdema, or œdema following paracentesis; but the paroxysmal and recurring type has been found almost if not quite exclusively in association with the three conditions named.

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[9] Diseases of the Organs of Respiration, 1902, i, 242.

[10] Amer. Journ. Med. Sci., 1907, cxxxiii, 88; Trans. Assoc. Amer. Phys., xxi, 155.

So far as my own experience has been concerned, the cases have, with but one exception, been instances of cardiac, renal, or arterial disease attended with high blood pressure, and in the one exceptional case there was a cardiac lesion (mitral stenosis), and each attack of œdema was preceded by a nervous disturbance which doubtless temporarily elevated the systemic blood pressure. In some of the reported cases of recurring pulmonary œdema, unassociated with any of the three pathological conditions referred to, there have been other conditions—pregnancy (Riesman), nervous conditions (Levallée, Levy)—in which temporary or more continuous high pressure may have occurred.

The conditions which stand out most prominently in the cases that I have encountered have been increasing myocardial weakness and high arterial pressure. The occurrence of pulmonary œdema has, therefore, been more common in cases of myocardial than of valvular disease, and in cardiac disease associated with nephritis and arteriosclerosis than in the absence of such an association. The possible significance of these facts may be left for further discussion until the data of experimental investigation have been detailed.

2. *Experimental and Physiological Data.* Professor Wm. H. Welch,[11] in 1878, published the results of some experimental studies which have thrown a great deal of light on the pathogenesis of sudden pulmonary œdema. After reviewing various earlier theories he reports his experiments, which were directed to the determination of the possibility of producing pulmonary œdema by obstructions to the outflow of blood from the pulmonary circulation. Some preliminary experiments showed that the adaptability of the heart and circulation is so great that ligation of several of the large branches of the aorta failed to interfere with the work of the left ventricle sufficiently to lower the systemic circulation notably or to occasion pulmonary congestion and œdema. Ligation of the root of the aorta itself or clamping the pulmonary veins did occasion such results, but these procedures cause violent obstructions

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[11] Archiv f. path. Anat. und Phys. 1878, lxxii, 375.

of the circulation such as have no analogies in ordinary disease. The crucial experiment, to which various less convincing ones led up, was one in which he was able to cause acute œdema of the lungs in rabbits by squeezing the left ventricle between his finger and thumb, thus partially paralyzing it. He concluded that acute pulmonary œdema is due to "a disproportion between the working power of the left ventricle and of the right ventricle of such a character that, the resistance remaining the same, the left heart is unable to expel in a unit of time the same quantity of blood as the right heart." He did not then deny the possibility of another explanation for collateral fluxion with œdema or for infectious œdemas, and in a recent statement (quoted by Meltzer, 1904) specifically admits that a larger proportion of the cases of pulmonary œdema than is generally supposed is due to inflammatory changes in the vascular walls. His earlier experiments, however, conclusively demonstrated the fact that a lessened output of blood from the left ventricle as compared with the right could occasion acute pulmonary œdema. It is of interest to note that in cases of marked interference with the systemic circulation, even involving the distribution of several of the large branches of the aorta, he did not obtain the same result, nor even a notable falling off in arterial pressure, a fact which can be explained only by the reserve power of the heart and the extraordinary capacity for adjustment of the vasomotor apparatus of the systemic circulation. This fact, I believe, has important clinical bearings in connection with the cases of paroxysmal œdema. It cannot be referred to any vasomotor adjustment in the pulmonary circulation, for the reason that the ligatures established mechanical obstructions in the peripheral circulation which, if not counteracted in the remaining peripheral circulatory pathways, must of necessity have caused eventual overfilling of the lungs despite any activity of the pulmonary vasomotors, if any such exist.

Sahli[12] criticised Welch's results adversely, giving two principal objections: (1) That in human cases of sudden œdema the pulse does not indicate paralysis of the left ventricle; and (2) that the pathological condition of the lungs is not that of congestive œdema. As to the first objection, Welch has pointed out that he had not claimed that complete paralysis of the left ventricle is necessary to the production of the result under consideration, and thinks that Sahli is in error in assuming that such a degree of paralysis is essential. A consideration of the physiological principles involved will easily prove the correctness of Welch's contention. Taking Tigerstedt's figures (and these are smaller than those given by other physiologists) for the average output at each systole of the right and left heart, 50 to 100 grams, and assuming that the left heart has lost one-twentieth of its working power, the result would be a retention in the left heart, and eventually in the pulmonary circulation of from 2.5 to 5 grams after each heart beat. In one minute, at a rate of 80 per minute, the amount of blood retained in the lungs would be from 200 to 400 grams. It is easy to see that the result must be a speedy overfilling of the lungs. That such a condition of affairs should take place in human disease presupposes that the vasomotor mechanisms of the peripheral circulation had for some reason become ineffective. A study of the cases in my series and others reported in the literature, shows that there is good ground for believing that such an inefficiency of the vasomotor mechanism had become established.

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[12] Archiv f. exper. Path. und Pharm., 1885. 19.

In answer to Sahli's second objection that the anatomical conditions of the lungs are not those of congestive œdema, Welch refers to his own microscopic studies in human cases which showed the existence of congestion, and notes that Sahli apparently relied on the pallid macroscopic appearance of the lungs, having seemingly made no microscopic examinations. Welch further states that microscopic examinations of lungs of pallid appearance often show marked hyperemia and diapedesis of red cells. I can confirm this statement from some recent studies of highly œdematous but pallid lungs after adrenalin injections. While denying the force of Sahli's contention so far as the acceptability of Welch's theory is concerned it may perhaps be true that the degree of œdema in some cases of acute pulmonary œdema of human beings is out of proportion to the degree of congestion. An increased permeability of the pulmonary vessels might perhaps be the explanation of a ready leakage of serum under conditions of but moderate overfilling of the pulmonary circulation. This point will be referred to later on.

Grossmann[13] and Löwit[14] also criticised Welch's conclusions. though there is no fundamental difference in the results of their experiments and Welch's. Grossmann caused pulmonary œdema by poisoning with muscaria, and found the left ventricle in a state of spasm with resulting venous hyperemia of the lungs. He believes these conditions contrary to what Welch had stated in his conclusions, having overlooked the fact that disproportion in the working capacity of the left and right ventricle and not loss of power in the left ventricle was the important fact. Spasm of the left ventricle (though according to Welch unlikely in human cases) could, therefore, produce the same results as loss of ventricular power. Löwit's experiments seemed to him to show that increased flow of blood into the lungs as well as diminished outflow are two necessary conditions. If this were correct, there would be no conflict with Welch's postulates, but other experimenters did not find an increased flow into the lungs a necessary condition.

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[13] Ztschr. f. klin. Med., xii.

[14] Ziegler's Beiträge, xiv, 401.

A study of the experiments of Welch, as well as of those who believed their results pointed to different conclusions, seems to show without question that acute pulmonary œdema may be caused by mechanical congestion of the lungs the result of disproportionate work of the right and the left ventricles. It has been mentioned before that increased permeability of the pulmonary vessels may be a subsidiary cause, and two theories regarding the development of such a condition may be mentioned. According to some authors (Bouveret, Dieulefoy, Riesman), toxic agents acting in some obscure fashion or through the vasomotor system occasion, in cases of nephritis, rapid œdema of the lungs somewhat in the same way as œdema of the glottis occurs in the same disease. So far as the vasomotor system is concerned, it is important to observe that physiologists are practically unanimous in denying the existence of such a mechanism in the pulmonary circulation. If any exists, its range of action is extremely limited and is certainly too restricted to permit of its having more than a subsidiary place in the etiology of pulmonary congestion or œdema. So far as the second possibility, that of some direct toxic increase of vascular permeability, is concerned, analogies drawn from studies of œdema in other parts of the body make it probable that such a factor is of some importance. The fact that the lung is in a measure an excretory organ, and possibly liable to injury when vicarious excretion takes place, must be considered as having weight.

Hewlett[15] quotes his colleague Martin in confirmation of his belief that protein fluid of the concentration seen in one of his cases (total solids, 6.72 per cent., of which 6.302 per cent. was protein and 0.418 per cent. salts) could not have been forced through the vessel walls by any pressure short of one likely to cause actual rupture of the walls. However the facts may be as to this case, direct experiments have sufficiently demonstrated the possibility of œdema mechanical in nature to the extent that any cause save the mechanical element was a negligible factor. This does not obviate the possibility that some injurious agent acting upon the vascular permeability may be a subsidiary factor in cases of spontaneous œdema in man.

This is in conformity with Leber's[16] experiment, in which it was shown that the cornea with an intact epithelium of the membrane of Descemet will stand a pressure of 200 mm. of mercury, whereas once that epithelium is removed, solutions readily filter through. Very similarly, Tigerstedt and Santesson[17] found that the freshly removed lung of a frog filled with 0.6 per cent. NaCl solution will stand a pressure of 14 mm. of mercury for several hours without any escape of the contained fluid, whereas the same lung killed by slight heat or by pouring in distilled water, or frog's bile, at once allows filtration.

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[15] Intercolonial Med. Jour. Australasia, 1908, viii, 611.

[16] Archiv f. Ophthal., 1873, xix, 125.

[17] Bighang. till K. Svensk. Vet. Akad. Stockholme, 1886, xi, No. 2.

In view of these facts, it may be accepted as probable that some increase of vascular permeability may be a subsidiary cause in cases of recurring pulmonary œdema, but it would seem unlikely that such a state of affairs could develop suddenly and as suddenly subside. A more reasonable view is that a temporary pulmonary engorgement acting in conjunction with an increased or established vascular permeability is the important cause.

The facts that have brought me to the conclusion that the mechanical element is predominant are the following: (1) Welch and others have demonstrated that sudden inadequacy of the left ventricle may in a purely mechanical fashion occasion acute pulmonary œdema by causing pulmonary congestion; (2) cases of recurring œdema have generally been cases in which there have been persistent high arterial pressure and increasing myocardial weakness; (3) the attacks are sudden in onset and usually of relatively short duration, following excitement in many instances and usually occurring at night; and (4) renal disease or other ascertainable sources of toxemia may be wanting in some cases.

The first of the points has been sufficiently discussed. As to the second, I wish to add that in the majority of cases under my own observation there has been a continuous high pressure, sometimes excessively high, and prior to the onset of the paroxysms of œdema evidence of failure of the left ventricle. Among these evidences may be noted some increase in the size of the heart (dilatation) and weakening of the apex impulse and heart sounds, cardiac irritability indicated by extrasystoles, and oppression or anginoid attacks. Later, sometimes as a result of fatigue or excitement, an attack of acute œdema of the lungs occurred, and following this repeated paroxysms at irregular intervals. In the cases in which excitement or effort preceded the attacks there has been primarily a violent paroxysm of palpitation, then weaker action of the heart and œdema of the lungs. This sequence of events was clearly distinguishable in several attacks I have witnessed. These events may be interpreted as indicating a sudden extra strain imposed upon a heart struggling for a long time against excessive peripheral pressure and deprived of the protection of an intact vasomotor mechanism. Sudden external stress in normal individuals is neutralized by the inherent reserve power of the ventricle and the capacity of the peripheral vasomotor mechanism to open the external vascular channels. In cases of long-standing high pressure, arterial disease, and myocardial weakness, the cardiac power is deficient and the vessels are incapable of prompt dilatation. Another explanation is possible in some cases, that is, that inadequacy of the coronary circulation may occasion sudden insufficiency of the heart muscle under physical strain or at times of naturally lowered cardiac power, as during sleep, without the coöperative effect of high pressure and failure of the peripheral vasomotor mechanism. Romberg[18] refers to such a condition of affairs in discussing attacks of cardiac asthma which he does not distinguish fundamentally from those of recurring pulmonary œdema. It is unnecessary to enter very fully into the question of such a distinction here, but I wish to state my entire agreement with Romberg's view. It is impossible to draw a sharp line of demarcation between cases of cardiac asthma and those of acute pulmonary œdema. Few of the former are unattended with œdema of some degree, and none of the latter are free of dyspnœa of the same type as occurs in typical cardiac asthma. The difference is one of degree only, and attacks of the two sorts may alternate in the same case.

Regarding the symptoms and etiology of cardiac asthma, Romberg states: "The cause of asthmatic attacks is generally a sudden weakness of the left ventricle, which causes intense congestion of the lungs and thus leads to extreme dyspnœa. The ventricular weakness is indicated also by marked rapidity, softness, and smallness of the pulse and frequently by irregularity and in the occasional development of dilatation of the heart. The congestion of the lungs is frequently followed by the exudation of œdematous fluid into the alveoli. This pulmonary œdema, which is indicated by small and large moist rales scattered over small or considerable areas of the lung, is a further occasion for dyspnœa. The patient often coughs up œdematous fluid which may be light or dark red or even brownish from admixture of blood and may be of considerable amounts in some cases.

"The sudden loss of power in one of the sections of the heart may be occasioned by sudden embolic occlusion of one of the large branches of the coronary artery, but is practically only met with in cases of coronary sclerosis or in cases of widespread cardiosclerosis involving the distribution of blood to numerous capillaries, even though this interference be of but a moderate grade. One may, perhaps, conceive of the attacks as due to the following condition of affairs: When the power of the heart fails or when, as a consequence of overexertion or during rest as in deep sleep, the tension in the coronary arteries falls below a certain point, the existence of sclerosis of the coronary vessels may occasion an inadequate supply of blood to the cardiac capillaries, as a result of which there must be great loss of muscular power."

While I cannot subscribe to this statement in all particulars, and especially to the view that attacks of cardiac asthma or acute pulmonary œdema are in the great majority of cases due to coronary sclerosis or cardiosclerosis affecting the cardiac vessels, the effect of exertion, exhaustion, and deep sleep on cardiac power seems to me undoubtedly of prime importance in the determination of attacks of acute pulmonary edema in those predisposed to such paroxysms by long-existing high arterial tension and myocardial weakness. Romberg's statements, however, indicate another possible source of such attacks in cases in which high peripheral tension has not necessarily been a predisposing factor.

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[18] Krankheiten des Herzens, second edition, p. 82.

In attempting to reach some conclusion as to the relative importance of toxic increase of permeability of the pulmonary blood vessels and of mechanical engorgement of the lungs resulting from deficiency of the left ventricle, I am especially impressed by the features of such cases as Case II of my series. In this case a woman with uncomplicated mitral stenosis and without evidences of renal disease has on a number of occasions during a period of ten or more years suffered attacks of sudden pulmonary œdema, most of these attacks having followed some emotional excitement. There was never any acute illness before the seizure, and the recovery on all occasions has been so speedy and complete that within twelve hours all signs have vanished. The closest inquiry has failed to indicate even the possibility of a gastro-intestinal toxemia from dietary indiscretions. The mechanical element alone remains in evidence. One could, of course, conceive of vasomotor influences if there were sufficient grounds for believing that an active vasomotor mechanism is present in the pulmonary circulation. In other cases in which a renal lesion existed, and in which on this account toxic influences require greater consideration, the rapid onset and subsidence of the pulmonary œdema are strongly opposed to the assumption that increased permeability of the vessels as a result of toxemia is a prime factor in determining the rapidly appearing and disappearing pulmonary lesion. On the other hand, a temporary weakening, under mechanical stress, excitement, or other influences, of the left ventricle, followed by restoration of equality of action of the two ventricles, could readily account for the event. The conclusion which I have reached is that the conditions outlined by Welch in his original paper are the important ones in cases of recurrent or paroxysmal œdema of the lungs.

TREATMENT. The prompt effect of a hypodermic injection of morphine in cases of cardiac asthma led me to use the same remedy in one of the earliest cases of paroxysmal pulmonary œdema that fell under my notice. The result was so striking that I have since pursued the same plan, and have found this so satisfactory that it has never thus far been necessary to employ any other remedy except as an adjuvant. Some of the cases in the present series had large numbers of attacks, and eventually died, but there never was any difficulty in controlling the attacks themselves with morphine alone or supplemented with other less important drugs. When the fatal termination occurred, it usually resulted from gradually increasing failure of cardiac compensation, as in Case I. In some of my cases atropine was combined with the morphine in the hypodermic injections, but on repeated occasions morphine alone was used to test the matter and was found quite as efficient as with the addition. Therapeutists have uniformly recommended atropine to cause a drying of œdematous conditions of the lung, and the drug has, therefore, suggested itself, although it is difficult to appreciate in what manner such an effect could be brought about. When it was used independently of morphine, I found that its effects were not striking, as, for example, in one of the cases in this series in which large doses of atropine were administered during the first attack and the duration of the seizure was eight hours. In a number of subsequent attacks of apparently equal severity, a single injection, or at most two injections of morphine, with small amounts of atropine, sufficed to break up the seizures within an hour. In a few instances it seemed to me that the injections of morphine with the addition of small amounts of atropine acted more satisfactorily than injections of morphine alone, but I have come to the very positive conclusion that the atropine is of very secondary importance, notwithstanding the fact that in the discussion of Riesman's paper by the Association of American Physicians[19] a number of those who took part spoke most favorably of this remedy, none, however, making any detailed reference to cases. The impression I gathered was that the remarks made were more or less off-hand and based upon the traditional applicability of this drug.

Among the few authors who have mentioned morphine as a remedy for cases of paroxysmal œdema, the most enthusiastic is Hewlett, whose experiences coincide exactly with my own. In one of his cases he used morphine followed by atropine, but found that the latter had no noticeable effect. In eight remaining attacks in the same patient he used morphine alone, and found the patient invariably comfortable and out of danger in from one-half to three-quarters of an hour. In another of his cases, during his absence, a medical colleague was called in and employed various restorative measures with little effect. Upon Hewlett's arrival, three hours after the onset, he immediately injected one-quarter grain of morphine, and within a half hour the patient was comfortable, quiet, and of good color.

The manner of action of morphine in these cases cannot perhaps be fully explained. There is undoubtedly in many of the patients an element of shock and mental disturbance which contributes to the severity of the symptoms and which may be mitigated by the injection of morphine. This view was expressed by Billings in the discussion of Riesman's paper. My experiences, however, in the treatment of many attacks in a number of patients leads me to doubt whether this explanation suffices for the very striking results obtained. If one may draw conclusions from cases of cardiac asthma in which the results of injections of morphine, with or without atropine, are so well known, and in which an element of bronchial spasm seems to exist, one may perhaps suspect that, though it is not so apparent, a similar condition of muscular spasm is also present in the cases of pure œdema, and that by relief of this, improvement is initiated. This might readily enough explain the cessation of active dyspnœa, but could not so well explain the rapid disappearance of the œdema itself. Having regard to the pathogenesis of paroxysmal pulmonary œdema and especially its probable dependence upon relative weakness of the left ventricle, the explanation of the value of morphine may be that it exercises a direct effect upon the heart itself, quieting and steadying it; and also may have a beneficial influence by quieting restlessness and relieving muscular spasm of the extremities which increase the flow of venous blood to the right heart and thus occasion a larger supply to the pulmonary circulation. It must be confessed, however, that no explanation that can be offered at present seems entirely adequate, and the value of the remedy must rest very largely upon clinical experience. A few experiments which I have made seem to confirm this. In these experiments I injected adrenalin solution into the ear vein of rabbits, causing pulmonary œdema within a few minutes. In some of the animals, injections of morphine were made immediately after the adrenalin and in others a similar injection of atropine was made following the adrenalin. In the cases in which morphine followed the adrenalin the onset of the œdema was delayed and its intensity decidedly less, though the animals eventually developed œdema and died. In the cases in which atropine was used there was an immediate onset of œdema, which was much more decided than in the cases in which adrenalin alone was used.

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[19] Trans. Assoc. Amer. Phys., 1906, xxi, 170.

Chloroform was used by Lissaman in his remarkable case in which seventy-two distinct attacks occurred. He found that he could control each of these in a very short time by inhalations of chloroform, finding that within ten to thirty minutes the patient became comfortable and was soon completely relieved. The effect of his treatment adds some confirmation to the opinion that the usefulness of morphine lies in its quieting effects. So far as the use of chloroform as a routine measure in such cases is concerned, it seems hardly likely that practitioners will generally be tempted to employ this remedy. The possible dangers of this drug in cardiac disease are too apparent to require further discussion.

Nitroglycerin has been frequently employed, and upon theoretical considerations may be regarded as indicated. If the pulmonary œdema is the result of a partial or considerable failure of the left ventricle, vasodilatation under the influence of nitroglycerin would undoubtedly prove useful by rendering the residual ventricular power more efficacious. In cases of cardiac asthma with moderate pulmonary œdema this result is not infrequently observed, but in the more serious cases of paroxysmal œdema my experience has been that nitroglycerin and the nitrites generally fail entirely. Possibly the explanation hinted at before may explain this failure, viz., that paroxysmal œdema occurs in cases of persistent high pressure and arteriosclerosis in which the vasomotor mechanism has been exhausted to the extent that vasodilatation, under the influence of drugs or as a result of natural reflex agencies when stress is brought to bear upon the left ventricle, has ceased to be available.

Venesection has been highly lauded, and naturally suggests itself when one observes a case of severe œdema with peripheral cyanosis. Merklen and Riesman advocate this plan of treatment above all others. Abstraction of blood from the venous system may undoubtedly relieve the pulmonary engorgement by diminishing the amount of blood flowing toward the right heart, and very probably it is in this manner that its usefulness is explainable. Compared to the simplicity of a hypodermic injection of morphine, venesection is a procedure of considerable gravity, and its effect cannot be more prompt or satisfactory.

After the first stage of the attack has been controlled by an injection of morphine and atropine, it is desirable to make use of cardiac stimulants to revive the power of the left ventricle and to promote vasodilatation, if this be possible. For these purposes injections of strychnine, digitalin, and nitroglycerin may be employed, and aromatic spirit of ammonia or brandy may be given by the mouth if the patient is able to swallow.

The after-treatment in cases in which one or more attacks have occurred consists in strict regulation of the daily life of the patient to avoid fatigue, excitement, cold, and physical strains, and some care of the diet so as to prevent overloading of the stomach and superalimentation, particularly at the evening meal. Renal cases may require warm or hot baths and particular care of the diet, and when myocardial weakness is evident after attacks, moderate cardiac stimulation may with advantage be used more or less continuously. On account of its action on the coronary circulation and on the kidneys, caffeine is a drug that may be particularly useful at this time; but strophanthus, digitalis, or nitroglycerin may be desirable.

In some of the cases under my care who had the constant attendance of a nurse I have left directions for (1) the immediate administration of aromatic spirit of ammonia upon the first suggestion of an attack, to be followed by (2) an injection of morphine sulphate, $\frac{1}{4}$ grain, with atropine sulphate, $\frac{1}{250}$ grain, when the first definite symptoms appeared; and (3) the subsequent repetition of morphine and atropine after fifteen minutes and later injections of strychnine and nitroglycerin. This plan served to control many threatening paroxysms before they had time to become severe.

THE CONTROL AND TREATMENT OF HYPERTENSION AND ARTERIOSCLEROSIS.

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There are a number of underlying facts which the diagnostician and the therapeutist must continue to bear in mind if he would successfully prevent the results of hypertension and influence the onward march of existing arteriosclerosis. To these facts I wish to allude.

Cardiovascular, more particularly arterial changes furnish the fundamental morbid processes in the largest number of deaths after the fortieth year. We are surprised when we examine our clinical material, more particularly that seen in private and consultation practice, to note the recent enormous increase of cardiovascular disease. We are promptly forced to the conclusion when this is compared with hospital statistics that there is an increase of the diseases of the arterial tree, coronary arteries, the myocardium, and in the nerve supply of the heart, the farther we are separated from hospital practice.

A careful study of the last 3200 cases of internal disease seen in private and consultation practice offers food for reflection. These include:

Arteriosclerosis	276
Endocarditis	135
Angina pectoris	44
Hypertension	67
Mitral obstruction	62
Aortic obstruction, vascular, endocardial (inflammatory)	151
Mitral insufficiency	267
Aortic insufficiency	20
Myocardial degeneration	277
Heart hypertrophy	63
Heart dilatation	59
Senile hearts	25

In a long-hand written report of the lectures of Benjamin Rush, which has recently fallen into my possession, that erudite clinician of enormous experience and supposed unlimited clinical material, makes the statement that in all of his experience he had seen but one case of angina pectoris, and he mentions the name of another physician practicing in Philadelphia who had also seen but one case.

Taking our clinical material into consideration, we are forced to the conclusion that hurry, worry, and excesses are at the bottom of a large majority of our cases in which we have degenerative changes in the cardiovascular system following a long or short period of hypertension. That heredity plays an important role in many of our cases we cannot deny, but we are equally positive that if these patients who are burdened with this unfortunate tendency were cautiously watched and correctly advised by the physician, changes of a degenerative nature in the heart and bloodvessels might be longer postponed. This is particularly true of arteriosclerosis as it affects the coronary and cerebral bloodvessels. It is not uncommon for us to get the history of three or four cases of coronary disease in one family, and we have family histories in which as many members of a family have died, either of cerebral apoplexy or of other brain disease associated with vascular anomalies.

These positive facts teach a valuable lesson. The study of the family history is too much neglected. Men who do not keep records, who do not question patients systematically, are very likely to overlook entirely the valuable facts which are gained by a thorough study of the patient's antecedents. These may seem rather commonplace remarks, but the consultant is so frequently brought face to face with these facts and understands so thoroughly their great importance that the opportunity to present them ought not to be neglected.

Modern pathology makes clear beyond peradventure the further fact that there is a physiological hyperplasia invading the intima during early life. We are forced to consider the separate artery as an organ, therefore, a part of the body which has positive functions to perform; that its task is not single but multiple, and that the performance of its daily undisturbed work is attended even during the earliest years of life with a compensatory deposit for the preservation of these organs and the continuity of the circulation. As soon as this physiological hyperplastic change of the intima because of age, overwork, strain, toxemia, or from any other causes is forced into a stage of hypertrophy, we have the beginning of arteriosclerosis.

There is a considerable period of hypertension which precedes this profound change in the arterial tree which, however, in the majority of cases is not recognized, because of a natural tolerance; and when present there is almost immediate compensation. If hypertension persists unrelieved and the factors which continue it remain uncontrolled, organic changes in vital organs are usually present, particularly in the heart, kidneys, and within the splanchnic area, before the patient presents subjective manifestations. In other cases, however, rather limited changes during the early days